SEGREGATION DISTORTION AND HETEROCLINIC CYCLES

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Bärbel Maria Regina Stadler

am Institut für Mathematik

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Abstract

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Deutsche Zusammenfassung

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1. Segregation Distortion

1.1. Mendel's Laws

The *Particulate Theory of Inheritance* was developed by Gregor Mendel, a member of the Königskloster at Bruenn in Moravia more than a century ago [32]. Mendel discovered two basic laws of inheritance which are named after him:

(1) No blending occurs when pure-bred individuals are crossed. Mendel found the proof by examining the first two daughter generations. The first consists of hybrid individuals, where either one of the characters may be obscured by the other, or some condition intermediate between the two characters defined the phenotype. In the second daughter generation, half of the population is composed of the original types in definite proportions, while the other half of the population are again hybrids. The term *segregation* was given to the recovery process of the original type in the second daughter generation.

(2) Two or more characters which are brought into the cross, segregate independently of each other. This principle is known as the law of *independent assortment*. In Mendel's examples (peas in the garden of the monastery) the two characters (color and texture of the flowers) were located on different chromosomes. The law of independent assortment is restricted to this situation. Otherwise the characters are *linked*.

In Mendel's days the mechanism which causes segregation was unknown. Mendel's results did not become popular before great advances had been made in cytology. It took almost thirty-five years until his results attracted general attention. By then it had become apparent that the hereditary material must be carried in the nucleus of the germ cells, for this is often the only part which the offspring receives from both its parents. Within the nucleus, the chromosomes had been found. They separate and recombine in a manner well fitted to provide the physical basis of the Mendelian segregation of characters [8].

1.2. Unfair Segregation

Segregation Distorters are genetic elements that exhibit the phenomenon of *meiotic drive*: that is, the mechanisms of the meiotic divisions cause one member of a pair of heterozygous alleles (*genic meiotic drive*) or heteromorphic chromosomes (*chromosomal miotic drive*) to be transmitted to progeny in excess of the expected Mendelian proportion of 50% [29]. They can be viewed as "ultra-selfish genes" since they not only show a tendency to increase in frequency without increasing the fitness of the organism harbouring them, but the driven element ("killer") achieves this increase by actively promoting the destruction of its allelic alternative(s) [9].

The distortion strength κ is the proportion of distorter alleles (resp. chromosomes) among all viable alleles (resp. chromosomes) trans mitted into progeny.

Segregation distorters can be further divided into two groups depending on whether they are *autosomal* or *sex-linked.* They occur in a wide range of organisms; table 1 lists a few examples. A comparison of a number of drive systems can be found in [29]. In this work we will restrict our attention to autosomal drive.

Table 1. Some Examples of Segregation Distorters in Nature.

Organism	Genetic Element	$\kappa^{\ddagger}$	Ref.
	Sex Ration Distortion		
Lemming, *Myopus schisticolor*	X-Chromosome	0.8	[13]
African Butterflies, Genera *Danaus, Acrea*	W-Chromosome	1.0	[6]
Mosquito: *Aedes aegyptii*	X-Chromosome	0.6*	[46]
Drosophila: subgroups *affinis* and *obscura*	X-Chromosome (SR)	†	[3]
Nasonia	PSR	?	[45]
	Autosomal Segregation Distortion		
Fungi, e.g. *Neurospora*	Spore Killer (Sk)	1.0	[43]
Mouse	t-haplotype (Chr. 17)	0.9 – 1.0	[39]
Drosophila *melanogaster*	SD-locus	0.95	[17]
Siberian Mouse	Chromosome 1	0.85	[1]
Maize	B Chromosome		[24]

*up to 1.0 in lab populations.
†many different subgenera with different distortion ratios.
‡The distortion strenght κ is explained in the text.

The first example of a segregation distorter system was found in several species of commensal mice, in particular in *Mus Domesticus* and *Mus Musculus.* It is a variant of chromosome 17 carrying an array of inversions called TRD ("transmission ratio distortion") which comprises roughly 1.2%

of the total mouse genome. Chromosomes carrying TRD have been termed t-haplotypes. Heterocygous t/+ males transmit predominately t-bearing sperm [39].

Segregation distorter chromosomes (SD) were discovered in 1956 in a natural population of *Drosophila melanogaster* by Y. Hiraizumi [21]. In males, they violate the Mendelian rule of segregation. Males heterozygous for *SD* produce progeny among which at least 95% carry *SD*. The mechanism of distortion is sperm dysfunction of a large fraction of the sperm carrying the genetically normal homologue of *SD*. Sandler and Novitski [35] proposed at about the same time that the rules of Mendelian transmission can be violated by a process they called *Meiotic Drive*.

Spore-Killer alleles (Sk) have been observed in various fungi, in particular in *Neurospora*. Sk/+ heterocygous fungi produce 50% viable spores which all carry Sk, while the other half of the spores are non-viable. This means that there is complete segregation distortion.

In *neurospora intermedia* two Spore-killer forms have been characterized, denoted $Sk-2_k$ and $Sk-3_k$. The spore killer $Sk-1_k$ was found in a different species, *neurospora sitophola*. Haploid Spore-killer strains of *neurospora intermedia* were originally identified because when crossed to a standard wild-type strain the eight-spore ascus deriving from Sk/+ diploid cells always carries four viable and four inviable spores. The four viable spores always carry Sk. This means that there is complete segregation distortion. For each spore killer there are both resistant and sensitive strains. Interestingly, some strains are $Sk-2_r$, but $Sk-3_s$ and vice versa, thus emphasizing the difference between the two Sk types.

B chromosomes are non-essential chromosomes which are present in some individuals of a population but not in others. They are never paired with a member of the normal (essential) chromosome set. B chromosomes occur both in diploids and polyploids, and they have been found in hundreds of species in all major taxonomic groups in both animals and plants. For a detailed survey of B chromosomes see ref.[25]. Supernumerary B chromosomes display probably the most common form of meiotic drive.

A comparison of mathematical models for the sex-ratio drive in *Drosophila Pseudoobscura*, the SD complex in *Drosophila Melanogaster*, the t-haplotype in *Mus Musculus*, and the sex-determination system in *Aedes Aegypti* can be found in ref.[12].

2. Model Dynamics

2.1. Replicator Equations

According to Dawkins [10] *replicators* are any entities that can get copied and satisfy the following two conditions:

(1) their properties can affect their proabability of being copied;

(2) the line of descendant copies is (at least in principle) unlimited.

A gene, for instance, is a replicator as long as it stays in the germ line.

Let x_i denote the relative concentration (frequency) of the replicator-species i. The dynamics of the relative concentrations is commonly described by the **replicator equation** [36]:

$$\dot{x}_k = x_k \left(\sum_{j=1}^{n} a_{kj} x_j - \sum_{i,j=1}^{n} a_{ij} x_i x_j \right) \ . \tag{$\mathcal{R}$}$$

In matrix notation this reads

$$\dot{x}_k = x_k \left[(Ax)_k - (xAx) \right] \ . \tag{$\mathcal{R}$}$$

Replicator equations arise in a variety of different fields. In sociobiology they are used to model the evolution of behavioral phenotypes [42], they model the dynamics of autocatalytic networks in macromolecular evolution

[11], Fisher's selection equations is of this form [8], they occur in theoretical immunology [41]; disguised as Lotka-Volterra equations they play a major role in mathematical ecology [34], and describe the mode selection in lasers [19].

The replicator equation stays the same if we substract a constant b_k in every column k of the corresponding matrix. So if we choose $b_k = a_{kk}$, then the resulting matrix is called game matrix of the replicator system. The entries in its k-th column are thus $a_{ik} - a_{kk}$ for all $i = 1, ..., n$. Hence, its main diagonal consists of zeros. We will call this the *normal form* of the game matrix.

Lemma 1. Let $\hat{x} \in \partial S_n$ be a fixed point and denote by K the set of all indices k for which $x_k = 0$. Then

$$\lambda_k := (A\hat{x})_k - (\hat{x}A\hat{x})$$

is the eigenvalue of the Jacobian of $\mathcal{R}$ belonging to the direction k. These eigenvalues are called *transversal*.

Proof. Trivial. ∎

A very useful observation is the following

Lemma 2. Let A be a game matrix in normal form. Then the entry a_{ki} is the transversal eigenvalue at the corner i belonging to the eigenvector pointing towards the corner k.

Proof. See, e.g., [23, p. 171]. ∎

2.2. Discrete versus Continuous Replicator Dynamics

In this section we investigate briefly the relation between the discrete-time replicator equation

$$x'_k = x_k \frac{(Ax)_k}{(xAx)} \tag{$\mathcal{R}^*$}$$

and the continuous time replicator equations

$$\dot{x}_k = x_k \left[(Ax)_k - (xAx)\right]. \tag{$\mathcal{R}$}$$

Lemma 1. Let $A > 0$. Then $(\mathcal{R})$ and $(\mathcal{R}^*)$ have the same rest points.

Proof. $A > 0$ implies $(xAx) > 0$ on S_n. The condition for x to be a rest point of $(\mathcal{R}^*)$ is $x'_k = x_k$, i.e., $x_k[(Ax)_k/(xAx) - 1] = 0$. Cleary, this is equivalent to the condition for x to be a rest point of $(\mathcal{R})$. ∎

It is not surprising that the Jacobian matrices J and J^* of $(\mathcal{R})$ and $(\mathcal{R}^*)$, respectively, are closely related. We have

Lemma 2. Let $\hat{x}$ be a rest point of $(\mathcal{R})$ and $(\mathcal{R}^*)$. Then

$$J^*(\hat{x}) = \frac{1}{(\hat{x}A\hat{x})} J(\hat{x}) + E,$$

where E denotes the matrix of identity.

Proof. The Jacobian for the continuous-time equation $(\mathcal{R})$ reads

$$J_{kl}(x) = \delta_{kl}\left[(Ax)_k - (xAx)\right] + x_k\left[a_{kl} - (Ax)_l - (xA)_l\right].$$

For the discrete-time equation $(\mathcal{R}^*)$ we find

$$J^*_{kl}(x) = \frac{1}{(\hat{x}A\hat{x})}\left[\delta_{kl}(A\hat{x})_k + \hat{x}_k a_{kl}\right] + \frac{1}{(\hat{x}A\hat{x})}\hat{x}_k\frac{(A\hat{x})_k}{(\hat{x}A\hat{x})}\left[(A\hat{x})_l + (\hat{x}A)_l\right]$$

Using that on a rest point we have $\hat{x}_k = 0$ or $(A\hat{x})_k = (\hat{x}A\hat{x})$ this reduces to

$$J^*_{kl}(\hat{x}) = \frac{1}{(\hat{x}A\hat{x})}\left\{\delta_{kl}(A\hat{x})_k + \hat{x}_k\left[a_{kl} - (A\hat{x})_l - (\hat{x}A)_l\right]\right\}. \tag{1}$$

Subtracting $(\hat{x}A\hat{x})$ from the first term inside the curly brackets yields $J^*_{kl}(\hat{x}) - \delta_{kl} = J_{kl}(\hat{x})/(\hat{x}A\hat{x})$. ∎

While the equilibria of $(\mathcal{R})$ and $(\mathcal{R}^*)$ do **not** have the same stability properties in general, we have the following useful result:

Lemma 3. Let $\hat{x}$ be a rest point of $(\mathcal{R})$ and $(\mathcal{R}^*)$ with $\hat{x}_k = 0$. Then the stability of the transversal direction k is the same for both equations.

Proof. First we observe that

$$\lambda^*_k(\hat{x}) = \frac{(A\hat{x})_k}{(\hat{x}A\hat{x})} > 0$$

as an immediate consequence of equation (1). Lemma 2 now implies that $\lambda_k(\hat{x})$ is greater than 0, equal to 0, and smaller than 0 if and only if $\lambda^*_k(\hat{x})$ is greater that 1, equal to 1, and smaller to 1, respectively. Hence the transversal direction k has the same stability for both dynamical systems. ∎

2.3. Two Sex Equation

In this section we derive the general form of the fertility selection equation for diploid populations, see e.g., [23, p.266]. Let x_k and y_k denote the frequencies of the male and female gametes, respectively. Let us first consider the discrete-time case. The fertility of male genotype $[ij]$ is m_{ij}, and correspondingly we denote the fertility of a female with genotype $[ij]$ by f_{ij}. We have:

$$\begin{aligned} x'_k &= \frac{1}{2\bar{m}}\left[x_k\sum_{j=1}^{n} m_{kj}y_j + y_k\sum_{j=1}^{n} m_{kj}x_j\right] \\ y'_k &= \frac{1}{2\bar{f}}\left[x_k\sum_{j=1}^{n} f_{kj}y_j + y_k\sum_{j=1}^{n} f_{kj}x_j\right] \end{aligned} \qquad (\mathcal{F}^*)$$

It will prove useful to consider the average frequencies of the gametes $z_k = (x_k + y_k)/2$, and the deviation from the averages $\delta_k = (x_k - y_k)$. For further usage we remark the converse transformation:

$$\begin{aligned} x_k &= z_k + \delta_k && \text{for the males, and} \\ y_k &= z_k - \delta_k && \text{for the females.} \end{aligned}$$

Using matrix notation, we can rewrite the fertility selection equation $(\mathcal{F}^*)$ as

$$\begin{aligned} x'_k &= \frac{1}{\bar{m}}[z_k(Mz)_k - \delta_k(M\delta)_k], \\ y'_k &= \frac{1}{\bar{f}}[z_k(Fz)_k - \delta_k(F\delta)_k]. \end{aligned}$$

From $\sum_j x_j = \sum_j y_j = 1$ we find immediately

$$\bar{m} = (zMz) - (\delta M\delta) \quad \text{and} \quad \bar{f} = (zFz) - (\delta F\delta).$$

The continuous analogue of this equation is obtained by means of the substitutions

$$2\bar{m}(x'_k - x_k) \to \dot{x}_k \qquad \text{and} \qquad 2\bar{f}(y'_k - y_k) \to \dot{y}_k.$$

This yields

$$\begin{aligned}\dot{x}_k &= x_k(My)_k + y_k(Mx)_k - 2x_k\bar{m}\\ \dot{y}_k &= x_k(Fy)_k + y_k(Fx)_k - 2y_k\bar{f}\end{aligned}$$

Two special cases of the "two sex equation" are of particular interest:

- If $M = F$, then the subspace

  $$R = \{(x,y) \in S_n \times S_n | x = y\},$$

  in which the sex ratio is equal, is invariant and globally attracting [23, p.268,Ex. 3]. The dynamics within this subspace is given by the discrete time replicator equation

  $$z'_k = \frac{z_k(Mz)_k}{(zMz)}.$$

- If there is no selection in one sex we find

  $$\begin{aligned}x'_k &= \frac{1}{\bar{w}}[z_k(Wz)_k - \delta_k(W\delta)_k]\\ y'_k &= z_k,\end{aligned}$$

  where x refers to sex which is subject to selection. This can be rewritten as

  $$\begin{aligned}2\bar{w}(z'_i - z_i) &= z_i(w_i - zWz) - [(\delta_i(W\delta)_i - z_i(\delta W\delta)]\\ 2\bar{w}(\delta'_i - \delta_i) &= 2\bar{w}(z'_i - z_i) - 2\delta_i\bar{w}\end{aligned}$$

which leads us to a slightly different construction of the continuous time analogue: replacing $2\bar{w}(z_i' - z_i)$ by $\dot{z}_i$ and $2\bar{w}(\delta_i' - \delta_i)$ by $\dot{\delta}_i$, respectively, yields

$$\begin{aligned}\dot{z}_i &= z_i[(Wz)_i - zWz] - [\delta_i(W\delta)_i - z_i(\delta W\delta)] \\ \dot{\delta}_i &= \dot{z}_i - 2\delta_i[(zWz) - (\delta W\delta)]\end{aligned} \tag{$*$}$$

In the following we will discuss a few general properties of the second special case as well as its relation to replicator equations.

Lemma 1. If $(\hat{x}, \hat{\delta})$ is a rest point of (*) then either $\hat{\delta}_i = 0$ or $\hat{\delta}_i = \pm\hat{x}_i$ for all i.

Proof. If $(\hat{z}, \hat{\delta})$ is a fixed point of (*) then

$$\hat{\delta}_i[\hat{z}W\hat{z} - \hat{\delta}W\hat{\delta}] = 0$$

and hence either $\delta_i = 0$ for all i or, if $\delta_i \neq 0$ for some i,

$$\hat{z}W\hat{z} = \hat{\delta}W\hat{\delta}. \tag{$**$}$$

It remains to investigate the implications of the condition (**). We know that $W > 0$ and $|\delta_i| \leq |z_i|$ for all i and all (z, δ). It is easy to see that (**) can be fulfilled only if $\delta_i = \pm z_i$, i.e., if one of the two sexes has dies out. ∎

Clearly the second class of equilibria is unrealistic: From the biological point of view the entire system has died out, the positive frequencies of some genotypes are merely artifacts of working with relative abundances.

We will therefore restrict attention to the case where $\delta = 0$. The gamete frequencies in equilibrium are determined by

$$z_i[(Wz)_i - zWz] = 0.$$

Note that the very same equation governs the rest points of the replicator equation

$$\dot{z}_i = z_i[(Wz)_i - zWz]. \tag{$\mathcal{R}$}$$

The relation between the continuous form of the model (*) and the replicator equation ($\mathcal{R}$) is even closer, however, as the following result shows:

Theorem. Let $(\hat{x}, \delta)$ be a rest point of (*), then $\hat{x}$ is a rest point of the replicator equation ($\mathcal{R}$) with the same fitness matrix. Furthermore, $(\hat{x}, 0)$ and $\hat{x}$ have the same number of non-negative eigenvalues.

Proof. The Jacobian of (*) has the components

$$\begin{aligned}
\frac{\partial \dot{z}_i}{\partial z_j} &= \frac{\partial}{\partial z_j}\{z_i[(Wz)_i - (zWz)]\} + \mathcal{O}(\delta) \\
\frac{\partial \dot{z}_i}{\partial \delta_j} &= \mathcal{O}(\delta) \\
\frac{\partial \dot{\delta}_i}{\partial z_j} &= \frac{\partial \dot{z}_i}{\partial z_j} - \mathcal{O}(\delta) \\
\frac{\partial \dot{\delta}_i}{\partial \delta_j} &= \mathcal{O}(\delta) - 2\delta_{i,j}(zWz)
\end{aligned} \tag{J}$$

At all meaningful rest points we have $\delta = 0$ and hence the Jacobian reduces to

$$\mathcal{J} = \begin{pmatrix} J & 0 \\ J & -2(\hat{z}W\hat{z})E \end{pmatrix}$$

where E is the identity matrix and J is the Jacobian of ($\mathcal{R}$), which has the entries

$$J_{ij} = \frac{\partial}{\partial z_j}\{z_i[(Wz)_i - (zWz)]\}\Big|_{z=\hat{z}}$$

It is easily to see that $-2(zWz)$ is an n-fold eigenvalue of $\mathcal{J}$. Consequently, the stability of the system is determined by the Jacobian of the replicator equation ($\mathcal{R}$). ∎

2.4. A Few Comments

We have now shown that the continuous form of the two-sex-fertility selection equation $\mathcal{F}$. In particular, if selection acts on only one sex, the equilibria of $\mathcal{F}$ and their stability are the same as for the replicator equation $\mathcal{R}$. The replicator equation can be interpreted as in terms of a strategic game that describes the genetic processes in a simpler form than $\mathcal{F}$. We use replicator equations in the following sections since more general models are often untractable, and it is difficult to predict their stability properties.

3. Heteroclinic Cycles

3.1. Heteroclinic Cycles in Biological Models

Definition. A *heteroclinic cycle* is a cyclic arrangement of saddle points together with connecting orbits such that each orbit has one saddle point as α-limit and the next one as ω-limit.

Heteroclinic cycles have not been very popular as ω-limits in biological models. Nevertheless they do occur in a number of simple models.

The simplest, though rather artificial, form of three dimensional equations that allow for heteroclinic cycles are those with circulant interaction matrices. A well-known example is the May-Leonard [30] model for cyclic competition which has attracted considerable interest, see e.g. [38, 33].

$$\dot{x}_1 = x_1(1 - x_1 - \alpha x_2 - \beta x_3)$$
$$\dot{x}_2 = x_2(1 - \beta x_1 - x_2 - \alpha x_3)$$
$$\dot{x}_3 = x_3(1 - \alpha x_1 - \beta x_2 - x_3)$$

where $0 < \beta < 1 < \alpha$, $\alpha + \beta < 2$. The assumptions behind this special Lotka-Volterra system are so artificial that is it unlikely that we could ever find them "in the field". Nevertheless they display very interesting features, and furthermore they yield handy analytical expressions that are easy to interpret. In the above case, there exists a unique interior rest point m given by

$$m_1 = m_2 = m_3 = 1/(1 + \alpha + \beta).$$

The Jacobian at m is circulant and it can be shown that m is a saddle. There are four further rest points, all on $\mathrm{bd}\mathbb{R}^3_+$, namely 0 (which is a source) and the three saddles e_1, e_2, e_3 which form an attractive heteroclinic cycle.

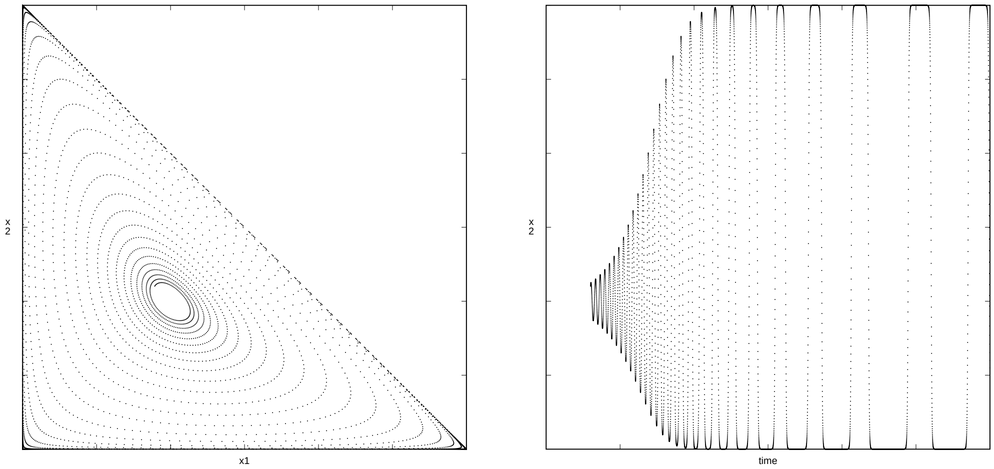

Figure 1: Example of a heteroclinic cycle. Replicator equation ($\mathcal{R}$) with the following interation matrix

$$A = \begin{pmatrix} 0 & -a & 1 \\ 1 & 0 & -a \\ -a & 1 & 0 \end{pmatrix}$$

with a=1.1. Left: phase portraits. Right: time evolution of x_2.

The Battle of the Sexes is an example of an asymmetric game due to Dawkins [10]. It models the conflict between males and females concerning their respective shares in parental investment. The corresponding differential equations are

$$\dot{x} = x(1-x)[C/2 - (G-E)y]\,,$$

$$\dot{y} = y(1-y)[-E + (C+E-G)x]\,,$$

where the parameters are non-negative pay-off values. For details see, e.g., [23, p.139f]. The state space for this relative of the Lotka-Volterra equation is the unit square $[0,1]\times[0,1]$. The edges of the square form a heteroclinic cycle. In Dawkin's original model displayed above the phase portrait consists of a continuum of periodic orbits surrounding a unique equilibrium in the interior of the square. Modifications of this model can lead to both an asymptotically stable and a repulsive heteroclinic cycle [37, 16].

Furthermore, heteroclinic cycles are abundant in hypercycle-like cooperation models [11, 2]. However, they are repulsive in all these systems. Andrea Gaunersdorfer [14, 15] has investigated heteroclinic orbits in replicator equations, focussing on the time-averages of the orbits.

3.2. Stability Concepts For Heteroclinic Cycles

The definitions given below are taken from [5]. They are based on the work of Ura and Melbourne [44, 31, 27].

Consider a flow on a subset $X \subseteq \mathbb{R}^n$.

Definition. "relative assymptotically stable"
Given any subset $N \subseteq X$, a closed invariant subset A of X is said to be *stable relative to the set* N or *stable in* N, if for every neighborhood U of A there is a neighborhood V of A, such that

$$\forall x \in V \cap N : x(t) \in U \forall t \geq 0.$$

A is said to be *asymptotically stable, relatively to N*, or *asymptotically stable in N*, if it is stable in N and there is a neighborhood V of A such that $\omega(x) \subset A \forall x \in V \cap N$, where $\omega(x)$ denotes as usual the ω-limit of x.
In the context of the work we will say that a heteroclinic cycle A is *relatively (asymptotically) stable* if there exists a set N such that A is (asymptotically) stable in N and $N \cap \mathrm{int} S_n \neq \emptyset$.

Definition. "essentially asymptotically stable"
A closed invariant subset A of X, is *essentially asymptotically stable in N* if it is relatively asymptotically stable to a set N which satisfies

$$\lim_{\epsilon \to 0} \frac{\mu(B_\epsilon(A) \cap N)}{\mu(B_\epsilon(A))} = 1,$$

where $B_\epsilon(A) =: \{x \in X | dist(x, A) < \epsilon\}$ and μ is the Lebesgue measure.
In this work we will say that a heteroclinic cycle is essentially asymptotically stable if it is essentially asymptotically stable in S_n.

3.3. Heteroclinic Cycles in the Plane

Notation. [5] Let Γ be a heteroclinic cycle consisting of the fixed points P_k, $k = 1, \ldots, 3$ and their connecting orbits. Then we use the following notation:

- e_k expanding (outgoing) eigenvalue at corner P_k;
- c_k contracting (incoming) eigenvalue at corner P_k;
- t_k^j transversal eigenvalue at corner k belonging to the eigenvector pointing in j direction. If there is only one transversal direction, then we drop the superscript and write simply t_k.

Furthermore we will make use of the abbreviations

$$\Pi_\Gamma = \prod_{k=1}^{3} e_k - \prod_{k=1}^{3} c_k, \quad \text{and}$$
$$\Delta_1 = t_1 e_2 e_3 + c_1 t_2 e_3 + c_1 c_2 t_3.$$

Δ_k for $k \neq 1$ is obtained by k cyclic permutations of the indices in Δ_1.

$$\Delta_k = t_k e_{k+1} e_{k+2} + c_k t_{k+1} e_{k+2} + c_k c_{k+1} t_{k+2}$$

where indices are taken modulo 3.

Theorem. [5, Proposition 3.1] Suppose Γ is lying in a 2-dimensional C^N-submanifold M of $\mathbb{R}^3$ and each connecting orbit is contained in the transverse intersection with a further 2-dimensional C^N-submanifold. If $Pi < 0$ and $\Delta_k < 0$ for $k = 1, \ldots m$, then Γ is relatively assymptotically stable. Conversely of $\Pi > 0$ or $\Delta_k > 0$ for one $k \in [1, m]$ then there is a neighborhood U of Γ and trajectory which eventually leaves U.

3.4. The 4-Cycle in S_4

On S_4, networks of heteroclinic cycles are possible; for example let us consider a flow which has two heteroclinic cycles Γ_1 and Γ_2 each consisting of three edges and corners which are hyperbolic saddle points.

Let $\Gamma_1 := F_1 \longrightarrow F_2 \longrightarrow F_3$, and $\Gamma_2 := F_1 \longrightarrow F_2 \longrightarrow F_4$. Let us label the eigenvalues at corner F_k of the cycle Γ_ℓ by $e_{k\ell}$, $c_{k\ell}$, and $t_{k\ell}$, for the unstable, stable and tranversal directions, respectively. See figure 2.

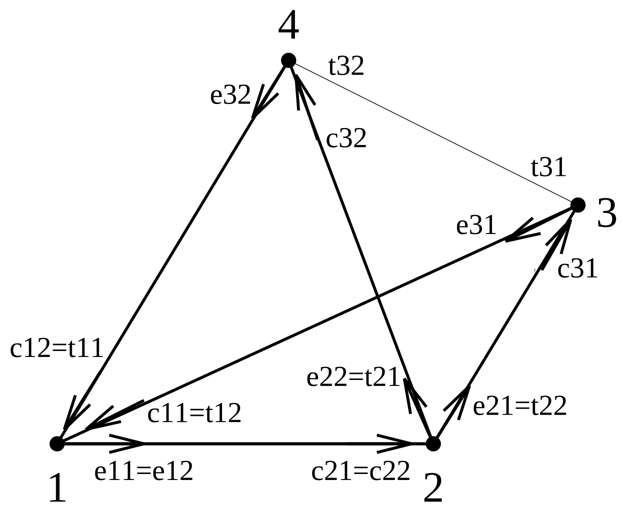

Figure 2: Notation for heteroclinic cycles on S_4.

From the Theorem above we know that Γ_ℓ is relatively asymptotically stable iff $\Pi_{\Gamma_\ell} < 0$ and each

$$\Delta_{k\ell} := t_{k,\ell}e_{(k+1),\ell}e_{(k+2),\ell} + c_{k,\ell}t_{(k+1),\ell}e_{(k+2),\ell} + c_{k,\ell}c_{(k+1),\ell}t_{(k+2),\ell} < 0,$$

where $k = 1, 2, 3$ is counted cyclically.

It is easy to check that $t_{1,l}, t_{3,l} < 0$ and $\Pi_{\Gamma_\ell} < 0$ implies

$$c_{3,\ell}\Delta_{1,\ell} < e_{3,\ell}\Delta_{3,\ell} \qquad \text{and}$$
$$e_{2,\ell}\Delta_{2,\ell} < c_{2,\ell}\Delta_{3,\ell}.$$

Brannath [5] showed the following

Theorem. (i) Γ_ℓ is relatively asymptotically stable if and only if $\Delta_{k,\ell} < 0$ for all k.
(ii) If both Γ_1 and Γ_2 are relatively asymptotically stable then Γ_1 is essentially asymptotically stable if and only $e_{11} > e_{12}$.

Results on more complicated networks containing a 4-cycle can be found in Brannath's work. We will not need them in this work.

4. One Locus Models

4.1. The Segregation Distorter Complex

The following model is originally due to Hiraizumi *et al.* [22]. Suppose we have a locus will allels D and d. The viabilities of the diploid genotypes are as follows:

$$\begin{array}{ccc} 1 & w_1 & D \\ w_1 & w & d \\ & & \\ D & d & \end{array}$$

The proportion of d-bearing gametes among all functional gametes produced by Dd is k. Let x_1 and x_2 denote the fraction of D and d gametes, respectively. The time-evolution of the population is described by a discrete or continuous time replicator equation with interaction matrix

$$W = \begin{pmatrix} w_{11} & 2(1-k)w_{12} \\ 2kw_{12} & w_{22} \end{pmatrix}.$$

The corresponding game matrix in normal form is

$$W = \begin{pmatrix} 0 & 2(1-k)w_{12} - w_{22} \\ 2kw_{12} - w_{11} & 0 \end{pmatrix},$$

and hence we have the following

Lemma. If

$2kw_{12} < w_{11}$ then $x_1 = 1$ is a stable equilibrium,

$2(1-k)w_{12} < w_{22}$ then $x_2 = 1$ is a stable equilibrium

$2w_{12} - w_{22} > 2kw_{12} > w_{11}$ then there is a globally stable polymorphic equilibrium with

$$\hat{x}_2 = (2kw_{12} - w11)/(2w_{12} - w_{11} - w_{22}).$$

Proof. For the discrete time model see [21]. The same results for the continuous time model follows, e.g., directly from ref. [11, p.44]. ∎

4.2. Mouse t-Haplotypes

Hartl [20] extended the above model to allow for different levels of meiotic drive in the two sexes. It is straight forward to extend his ansatz further to allow also for different viabilities in males and females, respectively. The most general model is then a two-sex equation $(\mathcal{F})$ with interaction matrices

$$M = \begin{pmatrix} m_{11} & 2(1-\phi)m_{12} \\ 2\phi m_{12} & m_{22} \end{pmatrix} \qquad \text{and} \qquad F = \begin{pmatrix} f_{11} & 2(1-\psi)f_{12} \\ 2\psi f_{12} & f_{22} \end{pmatrix}.$$

In natural populations of several species, especially in *Mus domesticus* and *Mus musculus*, a variant form of chromosome 17 has been identified that causes segregation distortion. These variants, the first of them was isolated more than 60 years ago, are now known as t-haplotypes, all having in common the property that heterozygous t/+ males transmit predominantly t-bearing sperm. The distortion ratio κ lies usually in the range 90-100%. The population dynmics of t-haplotypes was studied by Lewontin [28] assuming that (t/t) males are sterile and that segregation distortion occurs in males only.

This amounts to setting $\psi = 1/2$, $\phi = 1-\kappa$, $m_{22} = 0$, $m_{11} = f_{11} = 1$ and $m_{12} = f_{12}$ in the above interaction matrices. Karlin [26] showed that there is a globally stable equilibrium if $m_{12}(\kappa + 1/2) > 0$.

We could not find any heteroclinic cycles in this model.

5. Segregation Distorter in Drosophila Malanogaster

5.1. A Two Locus Case

Segregation distortion comprises a two-locus system of meiotic drive. On the killer locus alleles S (Killer) and $+$ (Non-Killer) are possible, while on the target locus, alleles R (Resistant) and $+$ (Non-Resistant) can be found. The resulting four gametic types are $++$, $+R$, $S+$, SR. With this notation SR is the Segregation distorter chromosome.

In *Drosophila melanogaster* segregation distortion occurs only in males, while recombination occurs only in females. Therefore, gametic frequencies can in general be different among the sexes.

5.2. The Model of Charlesworth and Hartl

The motivation for the following model is based on observations made on natural populations of *Drosophila Melanogaster*. Naturally occurring SR chromosomes usually carry a strong enhancer of distortion near the tip of the right arm of the chromosome and polygenic enhancers distributed along the whole right arm. The segregation ratio of $SR/++$ males is 95% or more, a ratio denoted in the matrix by k_1. Naturally occurring $+R$ chromosomes are not completely insensitive to such strongly distorting *SR* chromosomes; thus, *SR/+R* males produce about 80% *SR*-bearing offspring. This segregation ratio is denoted by k_3. The segregation ratio of *+R/S+* males is not known exactly, but it is around 60% in favor of *+R*.This segregation ratio is denoted k_2.

Charlesworth and Hartl [7] proposed the following matrix for male viabilities in their discrete-time model for the segregation distorter (*SD*) locus of *Drosophila Melanogaster*:

$++$	$+R$	$S+$	SR	
1	$1-s_1$	1	$2(1-k_1)(1-s_2)$ $=1-K_1$	$++$
$1-s_1$	$1-s_3$	$2k_2(1-s_2)$ $=1+K_3$	$2(1-k_3)(1-s_4)$ $=1-K_5$	$+R$
1	$2(1-k_2)(1-s_6)$ $=1-K_4$	1	$2(1-k_1)(1-s_2)$ $=1-K_1$	$S+$
$2k_1(1-s_2)$ $=1+K_2$	$2k_2(1-s_4)$ $=1+K_6$	$2k_1(1-s_2)$ $=1+K_2$	$1-s_5$	SR

Following ref.[7] we will argue below that in in populations of *Drosophila Melanogaster* only the genotypes $++$, *SR*, and *+R* play a role, and hence the dynamical model will be restricted to the face [++/*SR*/+*R*].

For the moment we will not make any assumptions on the values of the parameters $s_i > 0$ and K_i, $i = 1, \ldots, 6$. Our first observation in the general case is the following

Theorem 1. (i) There are at most two heteroclinic 3-cycles in the model (CH). A heteroclinic cycle lies either in the face $[{+}{+}/SR/{+}R]$ face or in the face $[{+}R/S{+}/SR]$. The heteroclinic cycle in $F_1{=}[{+}R/S{+}/SR]$ exists if and only if the heteroclinic cycle in $F_0{=}[{+}{+}/SR/{+}R]$ exists and the following two inequalities are fulfilled:

$$K_3 < 0 \qquad \text{and} \qquad s_3 > K_4.$$

(ii) Both can be stable within their faces, but at most one of them can be relatively asymptotically stable.

Proof. (i) Let $\lambda_i(x)$ and $\mu_i(x)$ denote the transversal eigenvalues pointing from the restpoint x to the corner i of in the faces $F_0{=}[{+}{+}/SR/{+}R]$ and $F_1{=}[{+}R/S{+}/SR]$, respectively. Heteroclinic cycles exist in these faces if and only if the following sets of inequalities for the parameters are fulfilled:

$$\begin{array}{ccc} \lambda_2(++) = -s_1 < 0 & \lambda_3(+R) = s_3 + K_6 < 0 & \lambda_1(SR) = s_5 - K_1 < 0 \\ \lambda_3(++) = K_2 > 0 & \lambda_1(+R) = s_3 - s_1 > 0 & \lambda_2(SR) = s_5 - K_5 > 0 \end{array}$$

$$\begin{array}{ccc} \mu_2(+R) = s_3 - K_4 > 0 & \mu_3(S+) = K_2 > 0 & \mu_1(SR) = s_5 - K_5 > 0 \\ \mu_3(+R) = s_3 + K_6 < 0 & \mu_1(S+) = K_3 < 0 & \mu_2(SR) = s_5 - K_1 < 0 \end{array}$$

The first group of inequalities reduces to

$$0 < s_1 < s_3 < -K_6, \;\; K_5 < s_5 < K_1 \;\; K_2 > 0.$$

The second group, referring to the other heteroclinic cycle can be simplified to

$$K_3 < 0 < s_1 < s_3 < -K_6, \;\; K_5 < s_5 < K_1 \;\; K_2 > 0, \;\; s_3 > K_4.$$

Hence both cycles exist whenever the second system of inequalities is fulfilled.

Since the edge [++/S+] is a line of fixed points there is no heteroclinic cycle in the faces [++/+R/S+] and [++/SR/S+]. This follows immediately from the classification of all possible phase portraits of the replicator equation by Immanuel Bomze [4].

A short calculation shows that the cycles are stable within their planes provided

$$K_2(s_5 - K_5)(s_3 - K_4) < K_3(s_3 + K_6)(K_1 - s_5) \text{ for } [+R/S+/SR], \text{ and}$$

$$K_2(s_5 - K_5)(s_3 - s_1) < s_1(-s_3 - K_6)(K_1 - s_5) \text{ for } [++/SR/+R].$$

Assume for instance $K_4 > -K_3 > s_1$. Then the above inequalities can be rewritten as

$$K_2(s_5 - K_5)(s_3 - K_4) < K_2(s_5 - K_5)(s_3 - s_1),$$

$$s_1(s_3 + K_6)(K_1 - s_5) < K_3(-s_3 - K_6)(K_1 - s_5),$$

and we conclude immediately that stabily of the heteroclinic cycle within [++/SR/+R] implies stability of the cycle in [+R/S+/SR].

(ii) Let as now turn to relative assymptotic stability. We have the following transversal eigenvectors:

$t_1 = 0$	$t_2 = s_5 - K_1 < 0$	$t_3 = s_3 - K_4 > 0$	[++/SR/+R]
$t_1 = s_3 - s_1 > 0$	$t_2 = 0$	$t_3 = s_5 - K_1 < 0$	[+R/S+/SR]

The conditions for relative asymptotical stability are therefore

$$\Delta_2([++/SR/+R]) = K_2(s_3 - K_4)(s_5 - K_1) - (s_5 - K_1)(s_3 - s_1)K_2 < 0$$

$$\Delta_3([+R/S+/SR]) = K_2(s_5 - K_1)(s_3 - s_1) - K_2(s_5 - K_1)(s_3 - K_4) < 0$$

Hence the heteroclinic cycle in [++/SR/+R] is relatively asymptotically stable for $s_1 < K_4$, while the heteroclinic cycle in [+R/S+/SR] is relatively

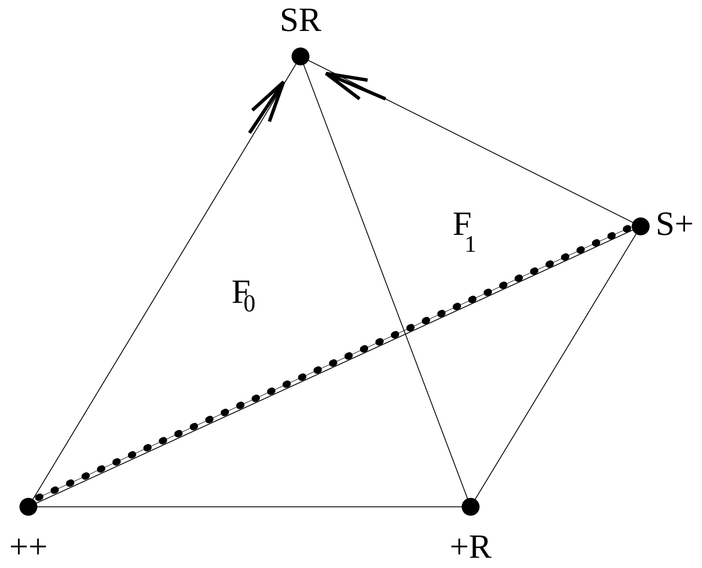

Figure 3: Heteroclinic cycles in the Charlesworth-Hartl model. The arrows indicate two eigenvalues at [SR] which are identical and hence prohibit the existence of a heteroclinic 4-cycle. Two heteroclinic 3-cycles are possible, in the faces F_0 (which corresponds to the model of Haig and Grafen discussed below) and F_1, see Theorem 5.2.1

asymptotically stable for $s_1 > K_4$, i.e., only one of them can be relatively asymptotically stable. ∎

Lemma. There is no heteroclinic cycle involving all four pure genotypes in the Charlesworth-Hartl model.

Proof. Since $[{+}{+}/S{+}]$ is a line of fixed points there are only two possible 4-cycles left, namely:

$$++ \rightarrow SR \rightarrow S+ \rightarrow +R \quad \text{and}$$

$$++ \rightarrow +R \rightarrow S+ \rightarrow SR$$

In the first case we require $s_5 > K_1$ for the expanding eigenvalue $SR{\rightarrow}S{+}$. However, the contracting eigenvalue $SR{\rightarrow}{+}{+}$ has to fulfil $s_5 < K_1$ in order to allow for the existence of a heteroclinic 4-cycle. The second case if the same cycle with the reverse direction, hence it cannot exist for the very same reason. ∎

5.3. Reduction to Three Species

Charlesworth and Hartl [7] argue that, *for biologically reasonable choice of the parameters*, all equilibria containing $S+$ either cannot exist or, if they exist, are unstable to the introduction of new gametic types. This conclusion is based on the following analytical results for the discrete-time replicator equation with the above interaction matrix. As a consequence of lemma 3 in section ??? these results hold for the continuous time model as well:

Theorem 1. For replicator equation ($\mathcal{R}$) with the Charlesworth-Hartl interaction matrix (CH) we have:

(1) The $S+$ corner is unstable to SR if $K_2 > 0$ and unstable to $+R$ if $K_3 > 0$.

(2) An $S+/SR$ marginal equilibrium is unstable to the introduction of $+R$ if $K_2(K_1 - K_5) + K_3(s_5 - K_1) > 0$. Since $K_5 < s_5 < K_1$ are realistic parameter values and K_2 can be fairly close to K_3, the equilibrium will be unstable in most cases.

(3) An $S+/+R$ equilibrium is unstable to the introduction of $++$ if $K_4 > s_1$.

(4) An $S+/++$ equilibrium is unstable to SR if $K_2 > 0$.

(5) An equilibrium on the $S+/SR/+R$ face is unstable to the introduction of $++$ if $K_4 > s_1$.

(6) The existence of an equilibrium on the $S+/+R/++$ face would require $K_4 = s_1$.

(7) An equilibrium on the $S+/SR/++$ exists if and only if $s_5 > K_1$ and $K_2 > 0$. It is unstable to $+R$ if

(a) $K_2(K_1 - K_5) + s_1(K_1 - s_5) > 0$ given that $K_3 > -s_1$, and

(b) $K_2(K_1 - K_5) - K_3(K_1 - s_5) > 0$ given that $K_3 < -s_1$,

(8) No equilibrium can exist within the $++/+R/S+/SR$ simplex, except for in the degenerate case $K_4 = s_1$, which is considered impossible.

(9) A stable $++/+R/SR$ equilibrium is stable to the introduction of $S+$ if $K_4 > s_1$.

Proof.(1) through (8) follow immediately from Charlesworth and Hartl's paper [6] and lemma 3 in section 2.2.

(9) We observe that

$$\Lambda_3(++/+R/SR) = (A\hat{x})_3 - (\hat{x}A\hat{x}) = (A\hat{x})_3 - (A\hat{x})_1 = (s_1 - K_4)\hat{x}_2. \quad \blacksquare$$

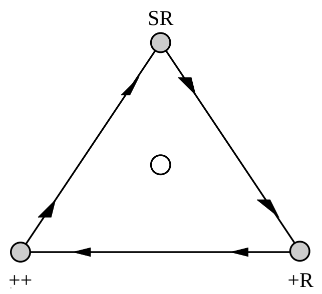

Figure 4: The heteroclinic cycle corresponding to the model of Haig and Grafen.

Remark. Result (8) implies that therefore that all trajectories of the continuous-time version of the Charlesworth-Hartl model converge to the boundary of the simplex. This is an immediate consequence of the *exclusion principle* [23, p. 64].

Assuming hence that $S+$ is non-viable and can be neglected therefore, we obtain the following three species model:

$$A = \begin{pmatrix} 1 & 1-s_1 & 1-K_1 & ++ \\ 1-s_1 & 1-s_3 & 1-K_5 & +R \\ 1+K_2 & 1+K_6 & 1-s_5 & SR \\ \\ ++ & +R & SR & \end{pmatrix}$$

Its game matrix reads:

$$A = \begin{pmatrix} 0 & s_3 - s_1 & s_5 - K_1 \\ -s_1 & 0 & s_5 - K_5 \\ K_2 & s_3 + K_6 & 0 \end{pmatrix}$$

As a consequence of Theorem 1 in the previous section there is a heteroclinic cycle if and only if

$$0 < s_1 < s_3 < -K_6, \;\; K_5 < s_5 < K_1 \;\; K_2 > 0.$$

It is stable provided

$$K_2(s_5 - K_5)(s_3 - s_1) < s_1(-s_3 - K_6)(K_1 - s_5).$$

5.4. The Model of Haig and Grafen

Haig and Grafen [18] proposed a simple model with heritable targets assuming two loci, which they called *Killer* locus and *Target* locus, whose wild-type allels are *Non-Killer* and *Non-Resistant*, respectively. The idea is that an allele *Killer* can arise at the *Killer* locus that causes haploid products to die at the end of meiosis unless they carry an allel *Resistant* at the *Target* locus. The death of some haploid products is assumed to benefit the survivors in some way: either by the acquisition of resources from the dead haploids, or by reduction of competition for fertilizations. The possession of *Resistant* is assumed to impose a viability cost, as compared with its allel *Non-Resistant*. The model is based on an imaginary protist life cycle, in which haploid organisms occasionally meet and fuse. There are three chromosome types in the populations: *Killer-Resistant* (K), *Non-Killer-Resistant* (R), and *Non-Killer-Non-Resistant* (N). The fourth type *Killer-Non-Resistant* kills itself during the meiosis that might have created it. A variation of the model relaxing the last assumption is discussed in the next section.

The detailed assumptions of Haig and Grafen's model are the following:

(1) There is a viablility cost w for each *Resistant* allel involved in the meiosis.

(2) There is a cost v for each unsuccessful attempt to kill.

(3) The gain in viability obtained by the driving allel *Killer* is j compared to a $N{\times}N$ mating.

(4) When two K mate, their relative viability is k.

(5) In $K{\times}N$ matings the drive is 100% successful, i.e., no *Non-Resistant* gametes survive.

(6) Drive does not occur in matings involving R.

Standardizing the fitness of $N \times N$ as 1 and bringing the interaction matrix to normal form one obtains the following game matrix:

$$A = \begin{pmatrix} 0 & w & -k \\ -w & 0 & 1-k-v-2w \\ j & -v & 0 \end{pmatrix}$$

where $j, k, v, w > 0$.

Table 2. Correspondence of the Haig-Grafen and the Charlesworth-Hartl models for the SD system in *Drosophila melanogaster*

Charlesworth-Hartl	Haig-Grafen
Genotypes	
$+/+$	$[NK/NR] = N$
$+/R$	$[NK/R] = R$
S/R	$[K/R] = K$
$S/+$	$[K/NR]$ lethal
Viabilities	
$w_{++/++} = 1$	$w_{NN} = 1$
$w_{++/+R} = 1 - s_1$	$w_{NR} = 1 - w$
$w_{+R/+R} = 1 - s_3 < 1 - s_1$	$w_{RR} = 1 - 2w$
$w_{SR/++} = 1 + K_2$	$w_{KN} = 1 + j$
$w_{++/SR} = 1 - K_1$	$w_{NK} = 0$
$w_{+R/SR} = 1 - K_5$	$w_{RK} = 1 - v - 2w$
$w_{SR/+R} = 1 + K_6$	$w_{KR} = w_{RK}$
$w_{SR/SR} = 1 - s_5$	$w_{KK} = k$
Realistic Values	
$w_{++/SR} < w_{SR/SR} < w_{+R/SR}$	$w_{NK} < w_{KK} < w_{RK}$

In the following the most important properties of this model are summarized as follows:

Lemma. There is a heteroclinic cycle if $k + v + 2w < 1$.

Proof. See Haig & Grafen [18]. ∎

Theorem. The heteroclinic cycle is stable if and only if

$$1 - v - 2w > k > \frac{j}{v+j}(1 - v - 2w)\,.$$

Proof. The heteroclinic cycle is stable if the interior equilibrium is unstable and *vice versa*, see, e.g., [4], [40]. The theorem follows now immediately from Appendix A in [18]. ∎

In the special case $v = w = j$ the condition for the stability of the heteroclinic cycle reduces to $1 - 3w > k > (1 - 3w)/2$.

The model by Haig and Grafen is closely related to the earlier, and much more complicated model by Charlesworth and Hartl discussed in the previous sections, see table 2.

5.5. A Modified Model

The above model can be modified by assuming that the fourth chromosomal type *Killer-Non-Resistant* is not completely lethal; let us denote this species by S. S should behave like N in combination with any other Non-Killer, but a zygote carrying S should have only a fraction ϵ of the fitness of the corresponding zygote carrying N instead of S. In combination with Killer, we introduce a second parameter η with $0 \leq \eta \leq \epsilon$. The fitness matrix then reads:

$$B = \begin{pmatrix} 1 & 1-w & 0 & \epsilon \\ 1-w & 1-2w & 1-v-2w & \epsilon(1-w) \\ 1+j & 1-v-2w & k & \epsilon(1+j)-\eta \\ \epsilon & \epsilon(1-w) & \eta & \epsilon^2 \end{pmatrix}$$

We assume ϵ to be very small, so we can neglect the fitness of the SS genotype, i.e., we set $\epsilon^2 \to 0$.

Theorem 1. For $\epsilon < 2(v+k)/(1+v+k) < 1 - w/(1-w)$ stability of the heteroclinic cycle in S_4 follows from stability of the heteroclinic cycle in the plane $[NRK]$.

Proof. Let $\lambda_i(x)$ denote the transversal eigenvalue pointing from the rest-point x to the corner i; we have

$$\begin{array}{ccc} \lambda_4(N) = \epsilon - 1 & \lambda_4(R) = \epsilon - 1 + w(2-\epsilon) & \lambda_4(K) = \eta - k \\ \lambda_1(S) = \epsilon & \lambda_2(S) = \epsilon(1-w) & \lambda_3(S) = \epsilon(1+j) - \eta \end{array}$$

It is easy to see that under the conditions of a stable heteroclinic cycle in the $[N/R/K]$ surface, and for all $0 \leq \eta \leq \epsilon$, we have

$$\lambda_4(N) < 0, \quad \lambda_1(S), \lambda_2(S), \lambda_3(S) > 0.$$

We have the following inequality in case of a heteroclinic cycle which is stable in its plane:

$$(1-v-2w) > k > j(1-v-2w)/(v+j). \qquad (*)$$

Let us transform this inequality such that the parameter is w.

$$(1-v-k)/2 > w > [j(1-v) - k(v+j)]/2j.$$

A sufficient condition for stability of the heteroclinic cycle in S_4 is that all the transversal eigenvalues are negative. We then require that

$$(\epsilon - 1) + w(2 - \epsilon) < 0 \text{ and } \eta - k < 0.$$

Let us assume the stronger $\epsilon - k < 0$. We then have $\epsilon < (1 - 2w)/(1 - w)$ and $\epsilon < k < (1 - v - 2w)$. We can also see that

$$\frac{\partial(1 - 2w)/(1 - w)}{\partial w < 0.}$$

From (*) follows that

$$\frac{[1 - 2(1 - v - k)/2]}{[1 - (1 - v - k)/2]} = 2\frac{v + k}{1 + v + k} < \frac{1 - 2w}{1 - w}.$$

The strongest inequality we can get is $\epsilon < 2(v+k)/(1+v+k) < (1-2w)/(1-w)$. This is a sufficient condition for the heteroclinic cycle to be stable in S_4. /par/noindent/bf Remark. For a relatively assymptotically cycle it is not necessary to require that all the transversal eigenvalues are negative. We will see this in the next chapter.

6. Competition of Killers

6.1. The Model

Let us consider model with two different Killer alleles K_1 and K_2. Then we have two alleles (R and $+$) at the target locus and three alleles ($+$, K_1, and K_2) at the killer locus. Thus there are six possible diploid genotypes. In order to reduce the model we make the following assumptions: (i) $+K_1$ and $+K_2$ are both lethal, and (ii) the two resistant genotypes RK_1 and RK_2 are (kinetically) indistinguishable and can hence be considered as single resistant genotype ALR. As in the model of Haig and Grafen $++$ is the sensitive genotype. The remaining two genotypes RK_1 and RK_2 are the two different killer strains K_1 and K_2, respectively. In order to reduce the number of free parameters we will assume additionally that the interaction with the resistant strain is the same for both killers. Thus we obtain the following game matrix:

$$A = \begin{array}{cc} & \begin{array}{cccc} R & N & K_1 & K_2 \end{array} \\ \begin{array}{c} R \\ N \\ K_1 \\ K_2 \end{array} & \begin{pmatrix} 1-2w & 1-w & 1-v-2w & 1-v-2w \\ 1-w & 1 & 0 & 0 \\ 1-v-2w & 1+j_1 & k_1 & k \\ 1-v-2w & 1+j_2 & k & k_2 \end{pmatrix} \end{array}$$

In normal form this becomes

$$A = \begin{pmatrix} 0 & -w & 1-v-2w-k_1 & 1-v-2w-k_2 \\ w & 0 & -k_1 & -k_2 \\ -v & j_1 & 0 & k-k_2 \\ -v & j_2 & k-k_1 & 0 \end{pmatrix}$$

General Assumptions.

(i) All the parameters in the above equation game matrix are positive: $j_1, j_2, k, k_1, k_2, v, w > 0$.

(ii) Without loosing generality we assume $k_2 \leq k_1$; that is, the viability of a K_2/K_2 genotype is less or equal to the viability of a K_1/K_1 genotype.

(iii) Additionally we require that $k_1 < 1 - v - 2w$ for $k < k_1, k_2$ and $(k^2 - k_1 k_2)/(2k - k_1 - k_2) < 1 - v - 2w)$ for $k > k_1, k_2$.

Lemma. Under the General Assumptions above there is always a heteroclinic cycle in both the face $[RNK_1]$ and the face $[RNK_2]$.

Proof. In $[RNK_1]$ there is a heteroclinic cycle if $1 - v - 2w - k_1 > 0$, which is exactly the condition above. Furthermore, for $k < k_1, k_2$, $(k^2 - k_1 k_2)/(2k - k_1 - k_2) < k_1$ holds, whereas for $k > k_1, k_2$, $(k^2 - k_1 k_2)/(2k - k_1 - k_2) > k_1$ holds, so that the strongest condition for the existence of a heteroclinic cycle stays $k_1 < (1 - v - 2w)$. For $k > k_1, k_2$, $(k^2 - k_1 k_2)/(2k - k_1 - k_2) > k_1$ holds, so that with $(k^2 - k_1 k_2)/(2k - k_1 - k_2) < (1 - v - 2w)$ we get a stronger condition for the existence of a heteroclinic cycle in the $[RNK_1]$ face.
In $[RNK_2]$ we need $1 - v - 2w - k_2 > 0$ which follows from $k_2 < k_1$. ∎

We distinguish two cases:

(I) $k_2 < k < k_1$. Then there is no equilibrium on the $[K_1,K_2]$ edge. There are two heteroclinic cycles.

(II) $k_2 < k_1 < k$ or $k < k_2 < k_1$. Then there is an equilibrium F on the $[K_1,K_2]$ edge. In this case there are at least three heteroclinic cycles. We will prove this statement explicitly in the next section for a special case. In general it follows from [4, 40] that there are trajectories connecting $N \rightarrow F$ and $F \rightarrow R$, and hence we have the three heteroclinic orbits $[RNK_1]$, $[RNK_2]$, and $[RNF]$.

6.2. The Symmetric Case: $j_1 = j_2$

In this section we will restrict ourselves to $j_1 = j_2$. Biologically, this means that the killer alleles K_1 and K_2 differ only in their interactions with themselves and with one another, but not with the sensitive and resistant strains S and R, respectively. In the next section we will relax this condition.

6.2.1. Case I: Two Heteroclinic Cycles

Let us assume that without loosing generality $k_2 \leq k \leq k_1$. Then there are two heteroclinic orbits, $[RNK_1]$ and $[RNK_2]$.

Theorem. (i) The heteroclinic cycle $[RNK_1]$ is relatively asymptotically stable under the general assumptions on the parameters if and only if $j(1 - v - 2w) < k_1$.
(ii) The heteroclinic cycle $[RNK_2]$ is never relatively asymptotically stable under the general assumptions on the parameters.

Proof. (i) Let us denote the expanding eigenvalues of the cycle by e_i, the contracting eigenvalues by c_i and the transversal eigenvalues by t_i, $i = 1, ..., 3$:

$$\begin{array}{rcc} e_1 = w & c_1 = v & t_1 = -v \\ e_2 = j & c_2 = w & t_2 = j \\ e_3 = 1 - v - 2w - k_1 & c_3 = k_1 & t_3 = k - k_1 \end{array}$$

The condition for stability for $[RNK_1]$ in the $[RNK_1]$-face reads

$$e_1e_2e_3 < c_1c_2c_3 \qquad \text{i.e.} \qquad j(1-v-2w)/(j+v) < k_1.$$

In order to prove relative asymptotic stability, we have to consider the signs of $\Delta_k(\Gamma_1)$ for k=1,2,3. $[RNK_1]$ is relatively asymptotically stable iff in addition to the equation above every $\Delta_k(\Gamma_1) < 0$. Thus the conditions for relatively asymptotically stability of $[RNK_1]$ are:

$$\begin{aligned} (k-k_1)vw &< 0, \\ j(1-v-2w) &< k_1(j+v) + w(k_1-k), \\ (k-k_1)jw &< 0. \end{aligned}$$

It is easy to see that all these equations hold if and only if $j(1-v-2w) < k_1$, and thus stability of the cycle $[RNK_1]$ in the whole system follows from stability in the $[RNK_1]$ face.
(ii) The condition for stability of the $[RNK_2]$ cycle in its face reads

$$j(1-v-2w) < k_2(j+v).$$

We get the following conditions for relatively asymptotically stability:

$$\begin{aligned} jw(k-k_2) &< 0, \\ vw(k-k_2) &< 0, \\ j(1-v-2w) &< k_2(j+v) + w(k_2-k). \end{aligned}$$

It is easy to see that the second and the third condition cannot 1 fulfilled since $k_2 < k$. Thus $[RNK_2]$ is not relatively asymptotically stable. ∎

6.2.2. Case II: Three Heteroclinic Cycles

Three heteroclinic cycles can occur if either $k_1, k_2 < k$ or $k_1, k_2 > k$

Lemma. The plane $Z = \{x \in S_4 | x_4(k - k_2) = x_3(k - k_1)\}$ is invariant.

Proof. It is easy to check that

$$\dot{x}_3(k - k_1) - \dot{x}_4(k - k_2) = [x_3(k - k_1) - x_4(k - k_2)] \cdot [jx_1 - vx_2 - (xWx)],$$

and hence Z is invariant. ∎

Now we introduce new coordinates

$$\begin{aligned} z &= \frac{1}{N}[(k - k_1)x_3 + (k - k_2)x_4] \\ d &= \frac{1}{N}[(k - k_1)x_3 - (k - k_2)x_4] \end{aligned}$$

where N is suitable normalization such that $z = x_3 + x_4$ on Z, i.e., $[(k - k_1)x_3 + (k - k_2)x_4] = N(x_3 + x4)$. Using $x_3 = x_4(k - k_2)/(k - k_1)$ we get

$$N = 2\frac{(k - k_1)(k - k_2)}{2k - k_1 - k_2}.$$

For convenience we give also the inverse transformation:

$$x_3 = \frac{k - k_2}{2k - k_1 - k_2}(z + d) \qquad x_4 = \frac{k - k_1}{2k - k_1 - k_2}(z - d).$$

We get the following system of differential equations:

$$
\begin{aligned}
\dot{x}_1 &= x_1\Bigg[-wx_2 + \frac{(1-v-2w-k_1)(k-k_2)+(1-v-2w-k_2)(k-k_1)}{2k-k_1-k_2}z+ \\
&\quad + \frac{(1-v-2w-k_1)(k-k_2)-(1-v-2w-k_2)(k-k_1)}{2k-k_1-k_2}d-(xWx)\Bigg] \\
\dot{x}_2 &= x_2\Bigg[wx_1 - \frac{k_1(k-k_2)+k_2(k-k_1)}{2k-k_1-k_2}z+ \\
&\quad - \frac{k_1(k-k_2)-k_2(k-k_1)}{2k-k_1-k_2}d-(xWx)\Bigg] \\
\dot{z} &= z\Bigg[-vx_1+jx_2+\frac{(k-k_1)(k-k_2)}{2k-k_1-k_2}z-(xWx)\Bigg]- \\
&\quad - \frac{(k-k_1)(k-k_2)}{2k-k_1-k_2}d^2 \\
\dot{d} &= d[-vx_1+jx_2-(xWx)]
\end{aligned}
$$

It is easy to see that for $d=0$ we have a system of replicator equations.

The coordinates of the fixed point F on the $[K_1]$- $[K_2]$ edge are

$$
\hat{x}_3 = \frac{k-k_2}{2k-k_1-k_2} \qquad \hat{x}_4 = \frac{k-k_1}{2k-k_1-k_2}.
$$

The fixed point F lies in the invariant plane Z defined above.

The game matrix for the system $[RNF]$ reads:

$$
A = \begin{pmatrix} 0 & -w & (1-v-2w)+(k_1k_2-k^2)/(2k-k_1-k_2) \\ w & 0 & (k_1k_2-k^2)/(2k-k_1-k_2) \\ -v & j & 0 \end{pmatrix}
$$

Let us denote the corresponding heteroclinic cycle $[RNF]$ by Γ_F. It is stable in its plane iff $\pi_{\Gamma_F} < 0$ There are two cases to distinguish:

(i) $k_2 \leq k_1 < k$, therefore $2k-k_1-k_2 > 0$, and

(ii) $k_1 \geq k_2 > k$, therefore $2k-k_1-k_2 < 0$.

CASE (i) $k_2 < k_1 < k$

Theorem. The heteroclinic cycle $[RNF]$ is stable in its plane iff

$$\frac{j}{j+v}(1-v-2w) < \frac{k^2-k_1k_2}{2k-k_1-k_2}.$$

Then it is also relatively asymptotically stable in S_4.

Proof. The condition for stability in the plane is simply $\Pi_{\Gamma_F} < 0$.
In order to determine the stability in S_4 we need to consider the Jacobian of the replicator system (***) for $d = 0$. All entries in the last row are 0, except the entry for $\frac{\partial \dot{d}}{\partial d}$ which is the transversal eigenvalue for a point in the face $[RNF]$. We have explicitly

$$\frac{\partial \dot{d}}{\partial d}|_{x_1=1} = -v\,, \qquad \frac{\partial \dot{d}}{\partial d}|_{x_2=1} = j\,, \qquad \frac{\partial \dot{d}}{\partial d}|_{z=1} = -\frac{(k-k_1)(k-k_2)}{2k-k_1-k_2}.$$

Therefore the relevant transversal eigenvalues are

$$t_1 = -v\,, \qquad t_2 = j\,, \qquad t_3 = -(k-k_2)(k-k_1)/(2k-k_1-k_2)\,.$$

Now we can apply Brannath's results [5, p. 25]:
Since $t_1 < 0$ and $t_3 < 0$ we have $e_3\Delta_3 > c_3\Delta_1$ and $c_2\Delta_3 > e_2\Delta_2$. Thus $\Delta_3 < 0$ implies already $\Delta_1, \Delta_2 < 0$, i.e., we have relative asymptotic stability iff

$$\Delta_3 = -\frac{(k-k_1)(k-k_2)}{2k-k_1-k_2} < 0$$

This inequality hold always in case (i). ∎

Remark. All three cycles $\Gamma_1, \Gamma_2, \Gamma_F$ are stable within their respective planes if

$$j(1-v-2w) < k_2(j+v),$$

because $k_2 = \min\{k_1, k_2, (k^2-k_1k_2)/(2k-k_1-k_2)\}$. Brannath's results imply immediately that neither Γ_1 nor Γ_2 can be asymptotically stable.

Case (ii) $k_1 > k_2 > k$

Theorem. The heteroclinic cycle Γ_1 is relatively asymptotically stable if it is stable in its plane, i.e., iff

$$j(1-v-2w) < k_1(j+v).$$

The heteroclinic cycle Γ_2 is relatively asymptotically stable if it is stable in its plane, i.e., iff

$$j(1-v-2w) < k_2(j+v).$$

Proof. Γ_1 is stable in its plane iff $\Pi_{\Gamma_1} < 0$, i.e., iff $j(1-v-2w) < k_1(j+v)$. $\Delta_3(\Gamma_1) < 0$ is always true in case (ii). Furthermore, its is straightforward to check that $\Delta_3(\Gamma_1) < 0$ implies already $\Delta_1(\Gamma_1), \Delta_2(\Gamma_1) < 0$. The proof for Γ_2 is completely analogous. ∎

Remark. The heteroclinic cycle Γ_F is in its plane iff

$$j(1-v-2w) < (j+v)\frac{k^2 - k_1 k_2}{2k - k_1 - k_2}.$$

It is never relatively asymptotically stable, since

$$\Delta_1(\Gamma_F) = -\frac{(k-k_2)(k-k_1)}{2k-k_1-k_2} vw > 0.$$

All three heteroclinic cycles are stable within their respective planes provided

$$j(1-v-2w) < (j+v)(k^2 - k_1 - k_2)/(2k - k_1 - k_2),$$

since $(k^2 - k_1 k_2)/(2k - k_1 - k_2) = \min\{k_1, k_2, (k^2 - k_1 k_2)/(2k - k_1 - k_2)\}$.

Remark. Neither Γ_1 nor Γ_2 is essentially asymptotically stable w.r.t. S_4 since the invariant plane Z cuts the respective basins of attraction into two pieces, both with non-zero measure. In particular, the two cycles both attract a part of the neighborhood of the RN-edge with non-zero measure.

In case that both Γ_1 and Γ_2 are relatively asymptotically stable we find that

$$\begin{aligned} \{x \in \mathrm{int} S_n | d > 0\} &\rightarrow \Gamma_1 \\ \{x \in \mathrm{int} S_n | d < 0\} &\rightarrow \Gamma_2 \end{aligned}$$

6.3. The Asymmetric Case: $j_1 \neq j_2$

Consider the following game matrix:

$$A = \begin{pmatrix} 0 & -w & 1-v-2w-k_1 & 1-v-2w-k_2 \\ w & 0 & -k_1 & -k_2 \\ -v & j_1 & 0 & k-k_2 \\ -v & j_2 & k-k_1 & 0 \end{pmatrix}$$

We assume $w, v, k, k_1, k_2, j_1, j_2, 1-v-2w-k_1, 1-v-2w-k_2 > 0$. In this more general case with $j_1 \neq j_2$ we cannot derive an equation for an invariant manifold corresponding to Z above.

6.3.1. Case 1: System without equilibrium on the K_1/K_2-edge

In this case we have $k_1 > k > k_2$. Again we assume without loosing generality that $k_1 > k_2$. In this case we have two heteroclinic cycles Γ_1 and Γ_2. We use the following notation:

$$\begin{array}{rll} e_1(\Gamma_1) = w & c_1(\Gamma_1) = v & t_1(\Gamma_1) = -v \\ e_2(\Gamma_1) = j_1 & c_2(\Gamma_1) = w & t_2(\Gamma_1) = j_2 \\ e_3(\Gamma_1) = 1 - v - 2w - k_1 & c_3(\Gamma_1) = k_1 & t_3(\Gamma_1) = k - k_1 \end{array}$$

$$\begin{array}{rll} e_1(\Gamma_2) = w & c_1(\Gamma_2) = v & t_1(\Gamma_2) = -v \\ e_2(\Gamma_2) = j_2 & c_2(\Gamma_2) = w & t_2(\Gamma_2) = j_1 \\ e_3(\Gamma_2) = 1 - v - 2w - k_2 & c_3(\Gamma_2) = k_2 & t_3(\Gamma_2) = k - k_2 \end{array}$$

We have to distinguish the following sub-cases:

(i) $j_1 > j_2$ and

(ii) $j_1 < j_2$.

Relative asymptotic stability of Γ_i is implied by $\Pi(\Gamma_i) < 0$, and $\Delta_3(\Gamma_1) < 0$ and $\Delta_1(\Gamma_2) < 0$, respectively. It is easy to check that under these conditions $\Delta_k(\Gamma_i) < 0$ for $i = 1, 2$ and $k = 1, 2, 3$.

Lemma. Γ_1 is relatively asymptotically stable if

$$\frac{j}{j+v}(1 - v - 2w) < k_1 \quad \text{and} \quad \frac{kwj_1}{wj_1 + v(j_1 - j_2)} < k_1$$

Proof. Follows immediately from the definitions of $\Pi(\Gamma_1)$ and $\Delta_3(\Gamma_1)$. ∎

<u>CASE (i): $j_1 > j_2$</u>

Theorem. Γ_2 is never relatively asymptotically stable for case 1.i. Γ_1 is essentially asymptotically stable if it is relatively asymptotically stable.

Proof. We show that $\Delta_1(\Gamma_2) > 0$. Assume $\Delta_1(\Gamma_2) < 0$. This is equivalent to $(j_1 - j_2)(1 - v - 2w - k_2) < w(k_2 - k) < 0$, while both $j_1 - j_2 > 0$ –

by assumption 1.i – and $1 - v - 2w - k_2 > 0$ – which is necessary for the existence of the heteroclinic cycle Γ_2. ∎

Case (ii): $j_1 < j_2$

Lemma. If Γ_2 is stable within its plane, then Γ_1 is also stable within its plane.

Proof. The functions $\psi(j) = j(1-v-2w)/(j+v)$ is monotonically increasing in j for all $j, v, w > 0$. The heteroclinic cycles Γ_i, $i = 1, 2$ are stable within their planes iff $\psi(j_i) < k_i$. Assuming $\psi(j_2) < k_2$ we find immediately

$$\psi(j_1) < \psi(j_2) < k_2 < k_1,$$

and therefore Γ_1 is stable as well. ∎

Both cycles can be relatively asymptotically stable:

Example. It is easily checked that both Γ_1 and Γ_2 are relatively asymptotically stable for the following choice of parameters:

$$v = w = 1/10, \quad k_1 = 3/5, \quad k = 8/15, \quad k_2 = 1/2, \quad j_1 = 1/20, \quad j_2 = 1/5.$$

Corollary. If Γ_2 is relatively asymptotically stable, then it is already essentially asymptotically stable.

Proof. This follows immediately from $j_1 < j_2$.

6.3.2. Case 2: System with equilibrium on K_1/K_2-edge

Recall that $k_1 > k_2$. Here we have four different sub-cases to distinguish:

(i) $k_1 > k_2 > k$, $j_1 > j_2$

(ii) $k_1 > k_2 > k$, $j_1 < j_2$

(iii) $k > k_1 > k_2$, $j_1 > j_2$

(iv) $k > k_1 > k_2$, $j_1 < j_2$

The coordinates of the equilibrium F on the $[K_1K_2]$-edge are given by

$$\hat{x}_1 = 0, \quad \hat{x}_2 = 0, \quad \hat{x}_3 = \frac{k - k_2}{2k - k_1 - k_2}, \quad \hat{x}_4 = \frac{k - k_1}{2k - k_1 - k_2}.$$

The Dynamics in $[RK_1K_2]$

Let us first consider the dynamics on the face $[RK_1K_2]$; we have explicitly

$$\dot{x}_1 = x_1[(1 - v - 2w - k_1)x_3 + (1 - v - 2w - k_2)x_4 - (xWx)]$$

$$\dot{x}_3 = x_3[-vx_1 + (k - k_2)x_4 - (xWx)]$$

$$\dot{x}_4 = x_4[-vx_1 + (k - k_1)x_3 - (xWx)]$$

These equations are the same as in the symmetric case $j_1 = j_2$, since neither j_1 nor j_2 appears here. We can thus rewrite them in terms of z and δ, knowing that $L = \{\delta = 0\} \cap [RK_1K_2]$, the straight line connecting the fixed points R and F is invariant. On L the dynamics reduces to a replicator equation with game matrix

$$A^* = \begin{pmatrix} 0 & 1 - v - 2w + (k_1k_2 - k^2)/(2k - k_1 - k_2) \\ -v & 0 \end{pmatrix}.$$

Lemma. There is an equilibrium on the line $L = [RF]$ iff $(1 - v - 2w) < (k^2 - k_1k_2)/(2k - k_1 - k_2)$. It is always unstable.

Proof. A necessary and sufficient condition is for existence is that A^*_{12} and A^*_{21} have the same sign. $A^*_{21} < 0$ then implies instability. ∎

It may be useful to observe whether R and N are stable to the introduction of N.

Lemma. R is unstable to the introduction of N.

Proof. $\frac{\partial \dot{x}_2}{\partial x_2}|_{x_1=1} = w$.

<u>Existence of a Heteroclinic Cycle *NRF*</u>

There is no invariant plane for general x_2; As in the symmetric case, however, we can have three heteroclinic orbits.

Theorem. There is a heteroclinic cycle Γ_F=NRF if Γ_1, Γ_2 and F exist.

Proof. The transversal eigenvalues of F are

$$\begin{aligned}
\lambda_1^{(F)} &= \frac{\partial \dot{x}_1}{\partial x_1}|_F = (1-v-2w-k_1)\frac{k-k_2}{2k-k_1-k_2} + (1-v-2w-k_2)\frac{k-k_1}{2k-k_1-k_2} \\
\lambda_2^{(F)} &= \frac{\partial \dot{x}_2}{\partial x_2}|_F = -k_1\frac{k-k_2}{2k-k_1-k_2} - k_2\frac{k-k_1}{2k-k_1-k_2}
\end{aligned}$$

The existence of Γ_1 and Γ_2 implies $(1-v-2w-k_1) > 0$ and $(1-v-2w-k_2) > 0$. The existence of F implies that k, k_1, k_2 fulfill one of the relations (i) through (iv), and hence the fractions $(k-k_j)/(2k-k_1-k_2)$, $j = 1,2$ are positive. The classification of all possible phase-portraits of the 3-species replicator equation [4, 40] implies now that there are orbits connecting $N \to F$ and $F \to R$, respectively. The remaining connection $R \to N$ is shared with both Γ_1 and Γ_2. ∎

CASE (i)

Both cycles can be relatively asymptotically stable:

Example. Both Γ_1 and Γ_2 are relatively asymptotically stable for the following choice of parameters:

$$v = w = 1/10, \quad k_1 = 7/10, \quad k_2 = 7/12, \quad k = 1/12, \quad j_1 = 1/2, \quad j_2 = 1/3.$$

Theorem. If Γ_1 is stable within its plane then its is essentially asymptotically stable.

Proof. $\Delta_3(\Gamma_1) < 0$ if and only if $(k - k_1)wj_1 < k_1v(j_1 - j_2)$ which is always true in case 2.i. Hence Γ_1 is relatively asymptotically stable iff $\Pi(\Gamma) < 0$, i.e., iff it is stable in its plane. $j_1 > j_2$ implies immediately that it is even essentially asymptotically stable. ∎

CASE (ii)

Lemma. If Γ_2 is stable within its plane, then Γ_1 is also stable within its plane.

Proof. This is the same as the proof of the lemma in case 1.ii. ∎

Theorem. Γ_2 is essentially asymptotically stable iff it is stable within its plane.

Proof. $\Delta_3 < 0$ whenever Γ_2 is stable in its plane since $(k - k_2)wj_2 < vk_2(j_2 - j_1)$. Essential asymptotic stability follows then from $j_1 < j_2$. ∎

Both heteroclinic cycles can be relatively asymptotically stable.

Example. Both Γ_1 and Γ_2 are relatively asymptotically stable for the following choice of parameters:

$$v = w = 1/10, \quad k_1 = 6/10, \quad k_2 = 4/10, \quad k = 2/20, \quad j_1 = 1/15, \quad j_2 = 1/10.$$

Case (iii)

Theorem. Γ_2 is never relatively asymptotically stable.

Proof. $\Delta_1 < 0$ would imply $(j_1 - j_2)(1 - v - 2w - k_2) < (k_2 - k)w < 0$, contradicting the general assumption, i.e., the existence of Γ_2.

Example. Γ_1 is relative asymptotically stable for

$$v = w = 1/10, \quad k_1 = 3/5, \quad k = 5/8, \quad k_2 = 1/2, \quad j_1 = 55/100, \quad j_2 = 1/2.$$

Case (iv)

Lemma. If Γ_2 is stable within its plane, then Γ_1 is also stable within its plane.

Proof. This is the same as the proof of the lemma in case 1.ii. ∎

Theorem. Γ_1 is never relatively asymptotically stable.

Proof. $\Delta_1 < 0$ would imply $(j_2 - j_1)(1 - v - 2w - k_1) < (k_1 - k)w < 0$, contradicting the general assumption, i.e., the existence of Γ_1.

Example. Γ_2 is relative asymptotically stable for

$$v = w = 1/10, \quad k_1 = 7/8, \quad k = 3/4, \quad k_2 = 2/3, \quad j_1 = 1/8, \quad j_2 = 1/2.$$

7. Spore Killer in Neurospora Intermedia

7.1. Biological Background

In *neurospora intermedia* two Spore-killer forms have been characterized, denoted $Sk-2_k$ and $Sk-3_k$. The spore killer $Sk-1_k$ was found in a different species, *neurospora sitophola.* Haploid Spore-killer strains of *neurospora intermedia* were originally identified because when crossed to a standard wild-type strain the eight-spore ascus deriving from Sk/+ diploid cells always carries four viable and four inviable spores. The four viable spores always carry Sk. This means that there is complete segregation distortion. For each spore killer there are both resistant and sensitive strains. Interestingly, some strains are $Sk-2_r$, but $Sk-3_s$ and vice versa, thus emphasizing the difference between the two Sk types.

There are two types of spore killers, Sk^2 and Sk^3. (Sk^1 was found in a different species, *Neurospora Sitophila*). For each spore killer there are both resistant and sensitive strains: R^2 is resistant against Sk^2, but sensitive against Sk^3. Analogously, R^3 is always resistant against Sk^3 and it is sensitive against Sk^2. Strains that are resistant to both Sk^2 and Sk^3 are denoted by $\mathbb{R}$. Furthermore, there are strains that are sensitive to both Sk^2 and SK3.

Sk^2 and Sk^3 kill each other with probability 99.9%.

In the absence of Killer alleles, meiosis in *Neurospora Intermedia* is fair and the product of each mating are eight viable spores.

If *K2* mates with *K2*, the product are eight viable spores. Analogously, if *K3* mates with *K3*, all eight spores survive. In matings of *K2* with *R3* resp. *S* only the four *K2* bearing spores survive. Analogously, only the four *K3* bearing spores survive in matings of *K3* with *R2* resp. *S*. Furthermore, if *K2* and *K3* mate, they kill each other.

7.2. A Game Dynamical Model

We shall assume the fertility parameters k_2 and k_3 for the genotypes *K2*K2* and *K3*K3*, respectively. Furthermore, let us assume that the cost of an unsuccessful attempt to kill is v_2 for *K2* and v_3 for *K3*. Let w_2, w_3 and w be fertility costs for *R2*, *R3*, and *R*, respectively. Let j_2 and j_3 be the gain in fertility for *K2* and *K3* compared to matings between *S* and *S*.

The fitness matrix is therefore

K_2	R_2	K_3	R_3	R	S	
$8k_2$	$8(1-v_2-3w_2)$	0	$8(1+j_2)$	$8(1-v_2-w_2-w)$	$8(1+j_2)$	K_2
$8(1-v_2-2w_2)$	$8(1-2w_2)$	0	$8(1-w_2-w_3)$	$8(1-w_2-w)$	$8(1-w_2)$	R_2
0	$8(1+j_3)$	$8k_3$	$8(1-v_3-2w_3)$	$8(1-v_3-w_3-w)$	$8(1+j_3)$	K_3
0	$8(1-w_2-w_3)$	$8(1-v_3-2w_3)$	$8(1-2w_3)$	$8(1-w_3-w)$	$8(1-w_3)$	R_3
$8(1-v_2-w_2-w)$	$8(1-w_2-w)$	$8(1-v_3-w_3-w)$	$8(1-w_3-w)$	$8(1-2w)$	$8(1-w)$	R
0	$8(1-w_2)$	0	$8(1-w_3)$	$8(1-w)$	8	S

The game matrix equivalent to the above fitness matrix is

$$A=\begin{pmatrix} 0 & -v_2 & -k_3 & j_2+2w_3 & w-v_2-w_2 & j_2 \\ 1-v_2-2w_2-k_2 & 0 & -k_3 & w_3-w_2 & w-w_2 & -w_2 \\ -k_2 & j_3+2w_2 & 0 & -v_3 & w-v_2-w_3 & j_3 \\ -k_2 & w_2-w_3 & 1-v_3-2w_3-k_3 & 0 & w-w_3 & -w_3 \\ 1-v_2-w_2-w-k_2 & w_2-w & 1-v_3-w_3-w-k_3 & w_3-w & 0 & -w \\ -k_2 & w_2 & -k_3 & w_3 & w & 0 \end{pmatrix}$$

7.3. Existence of Heteroclinic Cycles

Definition. An edge [XY] is directed from X to Y, in symbols [X→Y], if the omega-limit of every orbit in [XY] is Y.

Lemma 1. Let $\lambda_Y(X)$ and $\lambda_X(Y)$ be the transversal eigenvectors at X and Y with eigenvectors in [XY]. Then [X→Y] if and only of $\lambda_Y(X) > 0$ and $\lambda_X(Y) < 0$.

Proof. This follows immediately from the classification of replicator equations with $n = 2$ in [11]. ∎

In order to simplify the classification below we will assume that appart from the global conditions

$$v, w, w_2, w_3, \ldots > 0,$$

we have in addition:

$$1 - .....$$

The latter conditions guarantee that the edges .... are directed. If the latter conditions do not hold, then these edges are not directed. There are not parameter values for with these edges could have the opposite direction. When we say "does not depend on the numerical values of the parameters" during the reminder of this section we always imply that the above conditions **do** hold.

The direction of edges are compiled in the matrix below. Here, a $\bullet$ refers to an edge containing an interior rest point, i.e., an undirected edge. Arrows refer to directed edges in the following way: $\swarrow$ means that the edge is directed from the entry of the row to the entry of column, $\nearrow$ means that the edge is directed in the other way round. A question mark refer to edges for which the orientation depends on the parameter values. Figure 5 gives a graphical description.

					From	
To	K_2	R_2	K_3	R_3	R	S
K_2	–	$\nearrow$	$\bullet$	$\swarrow$	?	$\swarrow$
R_2	$\swarrow$	–	$\nearrow$	$\nearrow$	?	$\nearrow$
K_3	$\bullet$	$\swarrow$	–	$\nearrow$	?	$\swarrow$
R_3	$\nearrow$	$\nearrow$	$\swarrow$	–	?	$\nearrow$
R	?	?	?	?	–	$\nearrow$
S	$\nearrow$	$\swarrow$	$\nearrow$	$\swarrow$	$\swarrow$	–

Since all edges with parameter dependent orientation contain R we can give a complete list of all heteroclinic cycles that are independent of the numerical values of the parameters. We find

3-cycles $[K2/R2/S]$, $[K3/R3/S]$, $[K2/R2/R3]$,

4-cycles $[K2/R2/K3/R3]$, $[K2/R2/R3/S]$,

5-cycles $[K2/R2/K3/R3/S]$, $[K2/R2/K3/R3/S]$.

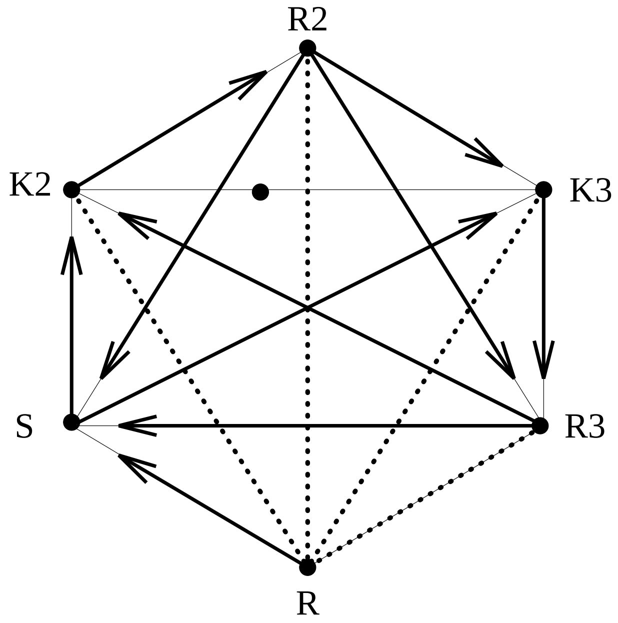

Figure 5: Direction of edges in the neurospora model. Unconditionally directed edges are indicated by arrows. The single unconditionally undirected edge is marked by a black dot, and dotted lines refer to edges with parameter dependent orientatation.

It remains to analyse the heteroclinic cycles containing R. Only the edge [RS] is determined independently of the numerical values of the parameters. We will show below that the remaining for edges containing R can have both directions, and that there are parameter values for each combination of directions.

Lemma. The directions of the edges containing R are determined by

$$\begin{array}{lcl}
R \to K2 & \Longleftrightarrow & ... \\
R \to R2 & \Longleftrightarrow & ... \\
R \to K3 & \Longleftrightarrow & ... \\
R \to R3 & \Longleftrightarrow & ... \\
K2 \to R & \Longleftrightarrow & ... \\
R2 \to R & \Longleftrightarrow & ... \\
K3 \to R & \Longleftrightarrow & ... \\
R3 \to R & \Longleftrightarrow & ...
\end{array}$$

Table 3. Heteroclinic Cycles involving R.

Edges	last			
first	K2/R	R2/R	K3/R	R3/R
R/S	R/S/K2 R/S/K3/R3/K2	R/S/K2/R2 R/S/K3/R3/K2/R2	R/S/K3 R/S/K2/R2/K3	R/S/K3/R3 R/S/K2/R2/R3 R/S/K2/R2/K3/R3
R/K2		R/K2/R2	R/K2/R2/K3 R/K2/R2/S/K3 R/K2/R2/R3/S/K3	R/K2/R2/R3 R/K2/R2/K3/R3 R/K2/R2/S/K3/R3
R/R2	R/R2/S/K2 R/R2/R3/K2 R/R2/K3/R3/K2 R/R2/R3/S/K2 R/R2/K3/R3/S/K2		R/R2/K3 R/R2/S/K3 R/R2/R3/S/K3	R/R2/R3 R/R2/K3/R3 R/R2/S/K3/R3
R/K3	R/K3/R3/K2 R/K3/R3/S/K2 R/K3/R3/S/K2/R2	R/K3/R3/K2/R2 R/K3/R3/S/K2/R2		R/K3/R3
R/R3	R/R3/K2 R/R3/S/K2	R/R3/K2/R2 R/R3/S/K2/R2	R/R3/S/K3 R/R3/K2/R2/K3 R/R3/S/K2/R2/K3 R/R3/K2/R2/S/K3	

This table can be used to determine all heteroclinic cycles that are consistent with a given set of parameters. This is done by determining whether an edge involving R is directed, and if so, if it is expanding or contracting. All cycles which are located in a column belonging to a contracting edge and in a row belonging to an expanding edge are present in the system. The conditions on the parameters are given in the text.

In table 4 we list all possible heteroclinic cycles as a function of their expanding (first) and contracting (last) edges at R. Since all edges except for those involving R do not depend on the numerical values of the parameters, the heteroclinic cycles in a box of table 4 exist if and only if the first edge is directed and expanding at R and the last edge is directed and contracting at R.

A stability analysis of the larger number of heteroclinic cycles which arise in the spore killer model presented above is, unfortunatly, beyond the scope of this *Diplomarbeit*, in part because very little is known about the stability of high dimensional heteroclinic orbits.

8. Conclusions and Open Questions

Heteroclinic orbits are an unusual type of attractor in models of biological processes.

[...]

One finds that there is a wealth of heteroclinic cycles in various models of unfair segregation, at least in part even for biologically sensible choice of interaction parameters.

[...]

The stability properties of the dozens of heteroclinic cycles appearing in the model for spore killers in neurospora and related fungi remain unknown. Little is known in general about the stability of heteroclinic orbits in S_n for $n \geq 5$.

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Table of Contents

Curriculum Vitae

BÄRBEL MARIA REGINA STADLER

*1966-05-13 in Mödling

Vater: Engelbert Duchkowitsch, Pensionist

Mutter: Ingrid Duchkowitsch (Hanauska), Hausfrau

⚭ Dr. Peter Florian Stadler, 1985-07-05

Kinder: Claus René, *1984-05-12, Manuel Ludwig, *1986-04-28

1972-1976	Volksschule Hirtenberg
1976-1984	Bundesgymnasium Berndorf
1984-**-**	Matura mit "Gutem Erfolg"
1986-1994	Universität Wien, Diplomstudium Mathematik.
19**-**-**	Erste Diplomprüfung.
1993-1994	Diplomarbeit bei Prof. Karl Sigmund

Publikation

[1] Stadler B.M.R. and P.F. Stadler: Dynamics of Small Autocatalytic Reaction Networks III: Monotonous Growth Functions. *Bull. Math. Biol.* **53**, 469-485 (1991).